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## A comparison of apremilast monotherapy and combination therapy for plaque psoriasis in clinical practice: A Canadian multicenter retrospective study

*To the Editor:* Apremilast is approved for treatment of moderate-to-severe plaque psoriasis (PP) as a monotherapy (MT). In clinical practice, it is sometimes used in combination therapy (CT) to manage residual PP that cannot be controlled with 1 agent alone. However, there are scant data comparing the real-world efficacy and safety of apremilast MT with those of CT.

We conducted a retrospective review of 148 patients at 2 academic centers in Toronto, Canada, to compare the real-world efficacy and safety of apremilast MT with those of CT. The study was approved by the research ethics board at Women's College Hospital and Sunnybrook Health Sciences Centre. The inclusion criteria were patients with PP who (1) used apremilast and (2) were at least 18 years old. CT was defined as apremilast treatment with phototherapy, systemic therapy, or biologic therapy. Patients receiving CT were screened to ensure that therapy other than apremilast had been used for at least 12 weeks before initiation of apremilast therapy to mitigate confounding efficacy and safety outcomes. Patients whose CT changed after addition of apremilast were excluded. All patients were permitted to use topicals. Efficacy (Psoriasis Area and Severity Index score of 75 or Physician Global Assessment score of 0 or 1) and safety (reported adverse events [AEs]) were assessed from baseline to week 16 (discontinuations were considered nonresponse). The Pearson chi-square test and Fisher's exact test were used to compare proportions, 2-tailed *t* tests were used to compare means, and logistic regression was used to compare efficacy and safety end points per the MT and CT cohorts, with a *P* value of 0.05 or less considered significant.

Baseline demographics (Table I) and efficacy and safety outcomes were summarized (Table II). Although not statistically significant, a greater proportion of patients receiving MT achieved a response than those patients receiving CT (26 of 59 who received MT [44.1%] vs 33 of 89 who received CT [37.1%] [$P = .396$]). This may be explained because patients receiving CT presented with more challenging psoriasis, as reflected by the higher proportion of patients with diabetes in their cohort ($P = .013$), which is associated with systemic treatment resistance and increased psoriasis severity.[1] Significantly more patients receiving CT had failed prior conventional systemic or biologic therapy ($P < .001$), further supporting their challenging presentation. The CT cohort also reported a significantly greater proportion of patients with psoriatic arthritis ($P < .001$) because apremilast is used in CT for both residual PP and for management of psoriatic arthritis.[2] Overall, both groups reported a proportionately appreciable clinical response compared with the 28.8% to 33.1% success rate of the ESTEEM clinical trials.[3,4]

Similar proportions of patients receiving MT and patients receiving CT experienced 1 or more AEs (37 of 59 who received MT [62.7%] vs 55 of 89 who received CT [61.8%] [$P = .911$]). Subgroup analysis of commonly reported AEs showed no significant difference between cohorts: headache ($P = .075$), diarrhea ($P = .796$), nausea ($P = .210$), and weight loss ($P = .486$). Many common AEs were reported in similar proportions within clinical trials, with the exception of upper respiratory tract infection and nasopharyngitis, which were not actively elicited at our centers.[3,4] One patient receiving CT experienced a severe AE and was admitted to the emergency department on account of significant acute weight loss; the weight loss stabilized and the patient continued treatment. These findings suggest that apremilast results in equally safe real-world outcomes, whether used as MT or used in CT.

Despite being limited by its retrospective nature, this real-world multicenter study suggests that apremilast can result in clinically significant reduction of PP, with primarily mild-to-moderate AEs, when it is used in clinical practice both as MT and in CT. Physicians may consider using apremilast as MT to control chronic PP or in CT to reduce residual PP that

**Table I.** Population demographics and baseline characteristics of study cohort

| Variable | Monotherapy (n = 59) | Combination therapy (n = 89) | All patients (n = 148) | *P* value |
|---|---|---|---|---|
| Male sex, n (%) | 34 (57.6) | 51 (57.3) | 85 (57.4) | .969 |
| Mean age (SD), y | 54.1 (12.0) | 51.5 (11.9) | 52.5 (12.0) | .193 |
| Mean disease duration (SD), y | 19.1 (14.2) | 20.7 (12.8) | 20.0 (13.4) | .598 |
| Comorbidities, n (%) | | | | |
| Psoriatic arthritis | 17 (28.8) | 51 (57.3) | 68 (45.9) | **<.001** |
| Hypertension | 18 (30.5) | 32 (36.0) | 50 (33.8) | .493 |
| Dyslipidemia | 12 (20.3) | 30 (33.7) | 42 (28.4) | .077 |
| Diabetes | 6 (10.2) | 24 (27.0) | 30 (20.3) | **.013** |
| History of malignancy | 15 (25.4) | 11 (12.4) | 26 (17.6) | .066 |
| Liver disease | 8 (13.6) | 16 (18.0) | 24 (16.2) | .475 |
| Psychiatric disorder | 9 (15.3) | 14 (15.7) | 23 (15.5) | .938 |
| Gastrointestinal symptoms | 5 (8.5) | 8 (9.0) | 13 (8.8) | .914 |
| Hypothyroidism | 4 (6.8) | 8 (9.0) | 12 (8.1) | .763* |
| Previously failed nontopical therapies, mean (SD) | 2.1 (1.6) | 3.6 (2.0) | 3.0 (2.0) | **<.001** |
| Failed therapies before apremilast, n (%) | | | | |
| Phototherapy | 43 (72.9) | 58 (65.2) | 101 (68.2) | .324 |
| Methotrexate | 30 (50.8) | 64 (71.9) | 94 (63.5) | **.009** |
| Acitretin | 20 (33.9) | 44 (49.4) | 64 (43.2) | .062 |
| Etanercept | 9 (15.3) | 44 (49.4) | 53 (35.8) | **<.001** |
| Adalimumab | 7 (11.9) | 32 (36.0) | 39 (26.4) | **.001** |
| Ustekinumab | 6 (10.2) | 27 (30.3) | 33 (22.3) | **.004** |
| Infliximab | 6 (10.2) | 13 (14.6) | 19 (12.8) | .429 |
| Cyclosporine | 2 (3.4) | 17 (19.1) | 19 (12.8) | **.005** |
| Alefacept | 2 (3.4) | 7 (7.9) | 9 (6.1) | .317* |
| Efalizumab | 0 (0.0) | 2 (2.2) | 2 (1.4) | .517* |
| Prior conventional systemic and/or biologic therapy, n (%) | 43 (72.9) | 84 (94.4) | 127 (85.8) | **<.001** |
| Prior conventional systemic therapy, n (%) | 39 (66.1) | 74 (83.1) | 113 (76.4) | **.017** |
| Prior biologic therapy, n (%) | 13 (22.0) | 60 (67.4) | 73 (49.3) | **<.001** |
| Combination therapies per patient, mean (SD) | — | 1.2 (0.4) | — | **—** |
| Combination therapies used by patients, n (%) | | | | |
| Methotrexate | — | 19 (21.3) | — | **—** |
| Etanercept | — | 18 (20.2) | — | **—** |
| Ustekinumab | — | 14 (15.7) | — | **—** |
| Adalimumab, methotrexate | — | 8 (9.0) | — | **—** |
| Infliximab | — | 7 (7.9) | — | **—** |
| Adalimumab | — | 5 (5.6) | — | **—** |
| Secukinumab | — | 3 (3.4) | — | **—** |
| Cyclosporine | — | 3 (3.4) | — | **—** |
| Ustekinumab, acitretin | — | 3 (3.4) | — | **—** |
| Phototherapy | — | 2 (2.2) | — | **—** |
| Infliximab, methotrexate | — | 2 (2.2) | — | **—** |
| Sulfasalazine | — | 2 (2.2) | — | **—** |

Proportions were compared by using the Pearson chi-square test or Fisher's exact test. Means were compared using a 2-tailed independent samples *t* test. Only comorbidities reported in at least 10 of all patients were listed. Only combination therapies reported in at least 2 of all patients were listed. Patients were permitted to be treated with combinations of biologics and apremilast because some health insurance plans in Canada cover this type of CT. In other cases, patients received compassionate doses of apremilast through Celgene Canada. Boldface indicates statistical significance.

*SD*, Standard deviation.

*Fisher's exact test was conducted instead of the Pearson chi-square test.